


U. S. Appln. No. 09/368,670
Supplemental Amendment

this issue. No new matter has been introduced by this amendment and entry thereof is therefore respectfully requested.


Applicants respectfully submit that this application is now in condition for allowance and earnestly request such action.

If any points remain at issue which can best be resolved by way of a telephonic or personal interview, the Examiner is kindly requested to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,


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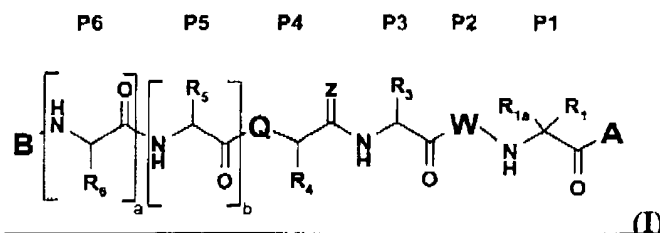
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Date: October 11, 2002

<p style="text-align: center;">Certificate of Transmission</p> <p>I hereby certify that this correspondence is being facsimile transmitted to the US Patent and Trademark Office to the following number: (703) 746-5071 on October 11, 2002.</p> <p style="text-align: center;"> Philip I. Datlow</p>
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MARKED-UP AMENDED CLAIMS

MARKED-UP COPY OF AMENDED CLAIMS

27. (Amended) The A compound of formula I according to claim 26;



wherein O is CH₂ or N-Y wherein Y is H or C₁₋₆ alkyl;

a) when Q is CH₂, a is 0, b is 0, and B is an amide derivative of formula R_{11b}N(R_{11b})-C(O)- wherein R_{11b} is H; C₁₋₁₀ alkyl; C₆ aryl; C₇₋₁₀ alkylaryl; C₃₋₇ cycloalkyl or C₄₋₈ (alkylcycloalkyl) optionally substituted with carboxyl; or heterocycle-C₁₋₆ alkyl;

and R_{11b} is C₁₋₆ alkyl substituted with carboxyl, (C₁₋₆ alkoxy)carbonyl or

phenylmethoxycarbonyl; or C₇₋₁₆ aralkyl substituted on the aromatic portion with

carboxyl, (C₁₋₆ alkoxy)carbonyl or phenylmethoxycarbonyl;

or R_{11a} and R_{11b} are joined to form a 3 to 7-membered nitrogen-containing ring optionally substituted with carboxyl or (C₁₋₆ alkoxy) carbonyl;

or

b) when Q is N-Y, a is 0 or 1, b is 0 or 1, and

B is an acyl derivative of formula $R_{11}-C(O)-$ or a sulfonyl of formula $R_{11}-SO_2$ wherein

~~R₁₁ is (i) C₁₋₁₀ alkyl optionally substituted with carboxyl or C₁₋₆ alkanoyloxy; C₁₋₆ alkoxy; or carboxyl substituted with 1 to 3 C₁₋₆ alkyl substituents;~~

(ii) C₃₋₇ cycloalkyl or C₄₋₁₀ alkylcycloalkyl, both optionally substituted with carboxyl,

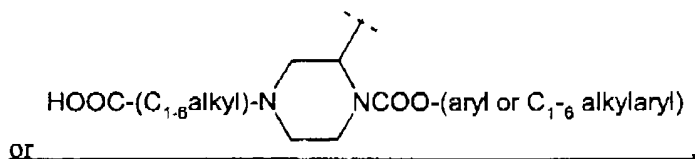
(C₁₋₆ alkoxy)carbonyl or phenylmethoxycarbonyl;

~~(iii) C₆ or C₁₀ aryl or C₇₋₁₆ alkyl optionally substituted with C₁₋₆ alkyl, hydroxy, or amino optionally substituted with C₁₋₆ alkyl; or~~

(iv) Het optionally substituted with C₁₋₆ alkyl, hydroxy, amino optionally

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substituted with C₁₋₆ alkyl, or amido optionally substituted with C₁₋₆ alkyl.



R₆, when present, is C₁₋₆ alkyl substituted with carboxyl;

R₅, when present, is C₁₋₆ alkyl optionally substituted with carboxyl;

and

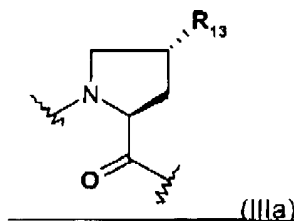
c) when Q is either CH₂ or N-Y, then

R₄ is C₁₋₁₀ alkyl, C₃₋₇ cycloalkyl or C₄₋₁₀ (alkylcycloalkyl);

z is oxo or thioxo;

R₃ is C₁₋₁₀ alkyl optionally substituted with carboxyl, C₃₋₇ cycloalkyl or C₄₋₁₀ (alkylcycloalkyl);

W is a group of formula IIIa:



wherein R₁₃ is o-tolylmethoxy; m-tolylmethoxy; p-tolylmethoxy; (4-tert-butyl)methoxy; (3I-Ph)CH₂O; (4Br-Ph)O; (2Br-Ph)O; (3Br-Ph)O; (4I-Ph)O; (3Br-Ph)CH₂O; (3,5-Br₂-Ph)CH₂O; or R₁₃ is OR₁₂ or SR₁₂ wherein R₁₂ is C₆ or C₁₀ aryl, C₇₋₁₆ aralkyl or Het, all optionally substituted with C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₁₋₆ alkoxy, acetylamido, nitro, CF₃, NH₂, OH, SH, halo, carboxyl, carboxy(lower)alkyl or a second aryl or aralkyl;

R_{1a} is hydrogen, and R₁ is the side chain of an amino acid selected from the group consisting of cysteine (Cys), aminobutyric acid (Abu), norvaline (Nva) and allylglycine (AlGly); or

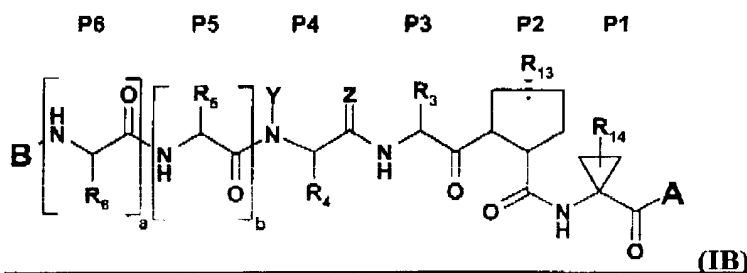
R_{1a} and R₁ together form a 3- to 6-membered ring optionally substituted with R₁₄ wherein R₁₄ is C₁₋₆ alkyl, C₃₋₅ cycloalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₆ aryl or C₇₋₁₀

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aralkyl all optionally substituted with halo; and

A is hydroxy; or C₁₋₆ alkylamino, di(C₁₋₆ alkyl)amino or phenyl-C₁₋₆ alkylamino;
wherein Het is a five-, six-, or seven-membered saturated or unsaturated, including
aromatic, heterocycle containing from one to four heteroatoms selected from nitrogen,
oxygen and sulfur, which heterocycle is optionally fused to a benzene ring;
or a non-toxic salt or ester thereof.

47. (Twice Amended) ~~The~~ A compound of formula IB according to claim 45,;



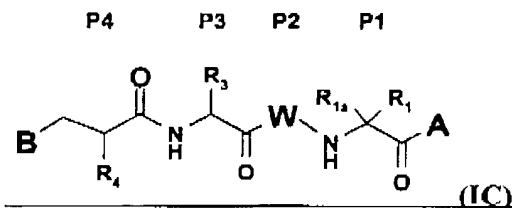
wherein B is an acyl derivative of formula R₁₁C(O)- wherein R₁₁ is C₁₋₆ alkyl; C₁₋₆ alkoxy; C₃₋₇ cycloalkyl optionally substituted with hydroxy; amido optionally substituted with C₁₋₆ alkyl or Het; C₆ or C₁₀ aryl, C₇₋₁₆ aralkyl or Het all optionally substituted with C₁₋₆ alkyl or hydroxy;

a, b, R₆, R₅, Y, R₄, Z, R₃, and A are as defined in claim 1.

R₁₃ is R₁₂, OR₁₂, C(O)OR₁₂, SR₁₂, NHR₁₂ or NR₁₂R_{12a} wherein R₁₂ and R_{12a} are as defined in claim 1; and

R₁₄ is C₁₋₆ alkyl, C₂₋₆ alkenyl optionally substituted with halogen; C₆₋₁₀ aryl or C₇₋₁₀ aralkyl optionally substituted with halogen; or a non-toxic salt or ester thereof.

68. (Twice Amended) ~~The~~ A compound of formula IC according to claim 67,;



wherein B is an amide of formula R_{11a}N(R_{11b})C(O)- wherein R_{11a} is C₁₋₆ alkyl; C₃₋₆

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cycloalkyl; C₃₋₇ (alkylcycloalkyl) optionally substituted with carboxy; C₁₋₃ carboxyalkyl;
C₆ aryl; C₇₋₁₀ arylalkyl; 2-tetrahydrofuranylmethyl; or 2-thiazolidylmethyl;
and R_{11b} is C₁₋₄ alkyl substituted with carboxyl;

R₄, R₃, W, R_{1a}, R₁, and A are as defined in claim 1.